

WHAT IS CLAIMED IS:

1. A bioactive implantable stent comprising a stent structure with a surface coating of a biodegradable, bioactive polymer, wherein the polymer comprises at least one bioactive agent covalently bound to the polymer, and wherein the at least one bioactive agent produces a therapeutic effect in situ.
2. The stent of claim 1, wherein the at least one bioactive agent is produced in situ as a result of biodegradation of the polymer.
3. The stent of claim 1, wherein the stent is sized for implanting in the vasculature and promotes endogenous wound healing processes at a site of implantation.
4. The stent of claim 1, wherein the at least one bioactive agent is selected to promote production of nitric oxide by endothelial cells at a locus of endothelial damage to a vessel and/or control proliferation of smooth muscle cells in the vessel at the locus of the damage.
5. The stent of claim 4, wherein the at least bioactive agent donates, transfers or releases nitric oxide, elevates endogenous levels of nitric oxide, stimulates endogenous synthesis of nitric oxide, or serves as a substrate for nitric oxide synthase.
6. The stent of claim 5, wherein the at least one bioactive agent is selected from arginine, lysine, aminoxyls, furoxans, nitrosothiols, nitrates, anthocyanins, sphingosine-1-phosphate, phospholipid lysophosphatidic acid.
7. The stent of claim 5, wherein the at least one bioactive agent is arginine.
8. The stent of claim 5, wherein the at least one bioactive agent is sphingosine-1-phosphate.

9. The stent of claim 5, wherein the at least one bioactive agent is phospholipid lysophosphatidic acid.
10. The stent of claim 5, wherein the at least one bioactive agent is an aminoxyl.
11. The stent of claim 10, wherein the aminoxyl is 4-amino-2,2,6,6-tetramethylpiperidinyloxy, free radical (4-Amino-TEMPO).
12. The stent of claim 1, wherein the polymer is polyester, poly(amino acid), polyester amide, polyurethane, or copolymers thereof.
13. The stent of claim 12, wherein the polyester is polylactide, polylactone, poly(α -hydroxy-carboxylic acid), poly(glycolic acid), or poly(3-hydroxybutyrate), or copolymers thereof.
14. The stent of claim 13, wherein said polylactone is polycaprolactone.
15. The stent of claim 1, wherein the bioactive agent is attached to the biodegradable, bioactive polymer via a linker.
16. The stent of claim 15, wherein the linker is a divalent radical of formula W-A-Q, wherein A is (C₁-C₂₄) alkyl, (C₂-C₂₄)alkenyl, (C₂-C₂₄)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀) aryl, and W and Q are each independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O), -S(O)₂-, -S-S-, -N(R)-, -C(=O)-, wherein each R is independently H or (C₁-C₆)alkyl.
17. The stent of claim 15, wherein the linker is a polypeptide comprising 2 up to about 25 amino acids.
18. The stent of claim 17, wherein said polypeptide is poly-L-lysine, poly-L-glutamic acid, poly-L-aspartic acid, poly-L-histidine, poly-L-ornithine, poly-L-threonine,

poly-L-tyrosine, poly-L-leucine, poly-L-lysine-L-phenylalanine, poly-L-arginine, or poly-L-lysine-L-tyrosine.

19. The stent of claim 15, wherein the linker separates the bioactive agent from the biodegradable, bioactive polymer by about 5 angstroms up to about 200 angstroms.

20. A bioactive vascular stent comprising a stent structure with a surface coating of a biodegradable, bioactive polymer, wherein at least one ligand for promoting re-endothelialization of endothelial cells is covalently bonded to the polymer.

21. The stent of claim 20, wherein the ligand is selected from peptides that promote endothelial cell growth.

22. The stent of claim 21, wherein the peptides that promote endothelial cell growth are selected from protein A and protein G.

23. The stent of claim 21, wherein the ligand is Protein A having an amino acid sequence as set forth in SEQ ID NO:1 or SEQ ID NO:2.

24. The stent of claim 21, wherein the ligand is Protein G having an amino acid sequence as set forth in SEQ ID NO:3 or SEQ ID NO:4.

25. The stent of claim 21, wherein the ligand is selected from bradykinins 1 and 2.

26. The stent of claim 20, wherein the polymer comprises polyester, poly(amino acid), polyester amide, polyurethane, or copolymers thereof.

27. The stent of claim 26, wherein the polyester is polylactide, polylactone, poly(α -hydroxy-carboxylic acid), poly(glycolic acid), or poly(3-hydroxybutyrate), or copolymers thereof.

28. The stent of claim 27, wherein the polylactone is polycaprolactone.

29. The stent of claim 20, wherein the bioactive agent is attached to the biodegradable, bioactive polymer via a linker.

30. The stent of claim 29, wherein the linker is a divalent radical of formula W-A-Q, wherein A is (C₁-C₂₄) alkyl, (C₂-C₂₄)alkenyl, (C₂-C₂₄)alkynyl, (C₃-C₈)cycloalkyl, or (C₆-C₁₀) aryl, and W and Q are each independently -N(R)C(=O)-, -C(=O)N(R)-, -OC(=O)-, -C(=O)O-, -O-, -S-, -S(O), -S(O)₂-, -S-S-, -N(R)-, -C(=O)-, wherein each R is independently H or (C₁-C₆)alkyl.

31. The stent of claim 29, wherein the linker is a polypeptide comprising 2 up to about 25 amino acids.

32. The stent of claim 31, wherein said polypeptide is poly-L-lysine, poly-L-glutamic acid, poly-L-aspartic acid, poly-L-histidine, poly-L-ornithine, poly-L-threonine, poly-L-tyrosine, poly-L-leucine, poly-L-lysine-L-phenylalanine, poly-L-arginine, or poly-L-lysine-L-tyrosine.

33. The stent of claim 29, wherein the linker separates the bioactive agent from the biodegradable, bioactive polymer by about 5 angstroms up to about 200 angstroms.

34. The stent of claim 1 or 17, wherein the stent is sized for intravascular insertion.

35. A tubular sheath comprising a biodegradable, bioactive polymer, wherein the polymer comprises at least one bioactive agent covalently bound to the polymer.

36. The sheath of claim 35, wherein the at least one bioactive agent is produced in situ as a result of biodegradation of the polymer.

37. The sheath of claim 35, wherein the biodegradable, bioactive polymer is elastomeric.

38. A bioactive implantable stent comprising a stent structure with a surface coating of a biodegradable, bioactive polymer, wherein the polymer produces a therapeutic effect in situ as a result of biodegradation of the polymer.

39. A biodegradable stent, wherein the stent comprises a crosslinked biodegradable polymer.

40. The biodegradable stent of claim 39, wherein the crosslinked biodegradable polymer is poly(caprolactone), poly(ester ether), poly(ester urethane), or a combination thereof.

41. A method for promoting natural healing of a damaged artery comprising implanting into the artery a stent according to claim 1 or 17 under conditions suitable for promoting natural healing of the artery.

42. The method of claim 41, wherein the natural healing comprises re-endothelialization of the artery wall.

43. A method of using a polymer as a medical device, a pharmaceutical, or as a carrier for covalent immobilization of a bioactive agent, wherein the polymer comprises at least one bioactive agent covalently bound to the polymer

44. The method of claim 43, wherein the at least one bioactive agent is produced in situ as a result of biodegradation of the polymer.

45. The method of claim 42, wherein the polymer coats an implantable medical device and the bioactive agent promotes natural wound healing processes in situ by contact with surrounding body area into which the medical device is implanted.

46. A bioactive implantable stent comprising:
a porous stent structure; and
a multilayered tubular coating encapsulating the stent structure, the multilayered coating comprising:
an outer drug-eluting biodegradable polymer layer, which sequesters an unbound drug; and
an inner layer of a biodegradable, bioactive polymer, wherein the polymer comprises at least one bioactive agent covalently bound to the polymer, and wherein the at least one bioactive agent produces a therapeutic effect in situ; and
an biodegradable barrier layer lying between and in contact with the outer layer and the inner layer and which barrier layer is impermeable to the drug.
47. The stent of claim 46, wherein the at least one bioactive agent comprises a ligand that promotes re-endothelialization of endothelial cells is covalently bonded to the inner polymer layer.
48. The stent of claim 47, wherein the ligand is selected from peptides that promote endothelial cell growth.
49. The stent of claim 48, wherein the peptides that promote endothelial cell growth are selected from protein A and protein G.
50. The stent of claim 48, wherein the ligand comprises Protein A having an amino acid sequence as set forth in SEQ ID NO:1 or SEQ ID NO:2.
51. The stent of claim 48, wherein the ligand comprises Protein G having an amino acid sequence as set forth in SEQ ID NO:3 or SEQ ID NO:4.
52. The stent of claim 47, wherein the ligand is selected from bradykinins 1 and 2.
53. The stent of claim 46, wherein the bioactive agent is attached to the biodegradable, bioactive polymer in the inner layer via a linker.

54. The stent of claim 53, wherein the linker is a polypeptide comprising 2 up to about 25 amino acids.

55. The stent of claim 54, wherein said polypeptide is poly-L-lysine, poly-L-glutamic acid, poly-L-aspartic acid, poly-L-histidine, poly-L-ornithine, poly-L-threonine, poly-L-tyrosine, poly-L-leucine, poly-L-lysine-L-phenylalanine, poly-L-arginine, or poly-L-lysine-L-tyrosine.

56. The stent of claim 46, further comprising an additional bioactive agent.

57. The stent of claim 56 wherein the additional bioactive agent is rapamycin, paclitaxel, everolimus, a statin, or an analog or derivative thereof.

58. The stent of claim 57, wherein the drug is hydrophobic and the barrier layer is less hydrophobic than the drug.

59. The stent of claim 57, wherein the drug is hydrophilic and the barrier layer is hydrophobic.

60. The stent of claim 58 or 59 wherein the polymer barrier layer comprises polyester, poly(amino acid), poly(ester amide), poly(esterurethane), polyurethane, polylactone, poly(ester ether), or copolymers thereof.

61. The stent of claim 46, wherein the stent is sized for intravascular insertion.

62. A method for promoting natural healing of an artery having an endothelium damaged by mechanical intervention comprising implanting into the artery immediately following the mechanical intervention a stent according to claim 1 or 46 under conditions suitable for promoting natural healing of the artery.

63. The method of claim 62, wherein the natural healing comprises re-endothelialization of the artery.

64. The method of claim 63, wherein the stent physically impairs activation of smooth muscle cells.

65. The method of claim 64, wherein the mechanical intervention is angioplasty.

66. The method of claim 62, wherein the mechanical intervention is balloon angioplasty.

67. The method of claim 62, wherein the method comprises implanting the stent to substantially cover a section of the interior artery wall damaged by the mechanical intervention.